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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

JUN 23 1986

EXPEDITE

MEMORANDUM

SUBJECT: PP#3F2897/FAB#3H5399 (RCB Nos. 1080 and 1081) - Pirimiphos-Methyl (Actellic®) on Stored Grains - Evaluation of Letter Dated June 12, 1986 (No Accession Number)

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and

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Note: This review has been expedited per the request of Mr. James Ackerman, Acting Registration Division Director (see memo of June 19, 1986 to Mr. John Melone, Hazard Evaluation Division Director).

ICI Americas, Inc., has written a letter dated June 12, 1986 to Dr. John Moore, Assistant Administrator for Pesticides and Toxic Substances, requesting help and assistance in resolving remaining issues impeding establishment of pirimiphos-methyl tolerances for residues in/on stored grains.

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ICI presents three major points which will be presented below, followed by RCB's comments/conclusions.

ICI Issue No. 1

ICI's primary concern involved TOX's lowering of the ADI (acceptable daily intake) (from 0.05 ppm initially; to 0.025 ppm on May 5, 1986; and to 0.01 ppm on May 22, 1986).

RCB's Comments/Conclusions re: Issue No. 1

RCB has no comments regarding this issue since it relates to special concerns of TOX.

ICI issue No. 2

"We believe that the calculated residues which result in exceeding 100% of ADI seriously overestimates actual residues for the following reasons:

A. Not all of the crop for which a tolerance has been established is treated with the pesticide.

B. Most treated crops have residue levels which are below the established tolerance levels.

C. Processing or time to market often result in further residue reductions.

D. Preparing food for consumption often results in residue reductions.

E. Not all crops contributing to the theoretical maximum residue contribution (TMRC) are likely to be consumed by an individual.

F. Market basket surveys conductd by FDA indicate that little, if any, real pesticide residues actually remain in/on food as consumed by the general population. For example, in the more than 75,000 samples which were analyzed by FDA, only about 1,300 samples showed findings greater than 0.01 ppm.

G. The TMRC and proposed tolerames for ACTELLIC include the hydroxypyrimidine metabolites which do not cause cholinesterase inhibition and therefore do not contribute to the NOEL which th ADI is based on.

[Reasons A-G are also used by the Agency in its rationale for permitting tolerances which exeed 100% of the ADI of the compound chlorpyrifos. (See "Guidance for the Reregistration of Pesticide Products Containing Chlorpyrifos," Environmental Protection Agency, September 28, 1984.) Reasons A, C, and D are used by the Agency in its tolerance justification for the stored gain insecticide chlorpyrifos-methyl. (See 50FR26684, June 27, 1985.)]"

RCB's Comments/Conclusions re: Issue No. 2

ICI has presented seven reasons above why the proposed tolerances ("calculated residues") overestimate actual residue levels. RCB's respones are presented below:

A. While it is true that "not all of the crop for which a tolerance has been established is treated with the pesticide," in the case of a stored grain (post-harvest) application such as that proposed in the subject petition, persons may consume a significant quantity of processed products prepared from a batch of treated grain. Since the chemical is applied such that the average level in the stored grain is the tolerance level, all of the grain will have residue levels approaching the tolerance.

B. Although "most treated crops have residue levels which are below the established tolerance levels," this would be generally true for pre-harvest pesticide uses, not post-harvest uses. For this stored grain use, the average level of residue in the treated grain will be tolerance level.

C. While "time to market" often results in residue reductions below the tolerance level, this is not the case for pirimiphos-methyl on stored grain. Pirimiphos-methyl is relatively stable on stored grains and decreases only around 30% after being stored for one year.

D. Processing and preparing food for consumption results in both residue reductions and increases in the case of pirimiphos-methyl. RCB has previously reviewed data concerning the effects of processing/baking on pirimiphos-methyl residue levels in various wheat grain products (see N. Dodd memo of April 10, 1980 re: PP#9G2200/ FAP#9H5217; J. Onley memo of January 20, 1984 and M. Firestone memo of June 20, 1986 re: PP#3F2897/ FAP#3H5399).

Based on analysis of these data, the following maximum concentration factors have been calculated:

Table I

Processed Wheat Commodity	Maximum Concentration Factor
bran	4.0
germ	7.1
whole meal flour	0.86
whole meal bread	0.61
white flour	0.37
white bread	0.26

Thus, persons eating wheat products prepared from treated grain could be exposed to a maximum of 4 to 7 times the pirimiphos-methyl application rate, which also reflects the proposed tolerance level, if bran or germ is consumed, or as little as about 1/4 or less the application rate if only white bread is consumed.

It should also be noted that there is little are no loss of residue on processing or baking for pirimiphos-methyl. The lower levels in bread are due to dilution of the flour with other ingredients in bread and are not due to degradation of the residue.

E. Although not all crops contributing to the theoretical maximum residue contribution (TMRC) are likely to be consumed by any given individual, the chances are increased that some people could consume products made from all the crops proposed for treatment with the subject petition since the crops are all cereal grains.

F. While FDA market basket surveys generally demonstrate actual residue levels in food well below established tolerances, this is less likely the case with post-harvest pesticide uses. To demonstrate whether this will be the case with stored grain use of pirimiphos-methyl, RCB could ask FDA to include this insecticide on its priority monitoring list if the proposed tolerances are established.

G. ICI states that "the TMRC and proposed tolerances for Actellic include the hydroxypyrimidine metabolites which do not cause cholinesterase inhibition and therefore do not contribute to the NOEL which the ADI is based on."

In response, ICI must be aware that treated grains stored for short intervals will contain residues composed of almost entirely cholinesterase inhibitors (parent compound plus its desethyl metabolite). Several plant metabolism studies carried out at high and low moisture content have been previously submitted. For example, considering just a few of the wheat and rice low moisture content studies, after 32 weeks (approx. 8 months) extractable residues on wheat grain consist of 79-86% parent compound, 9-11% of the 3 hydroxy-pyrimidine metabolities, 5-10% desethyl pirimipos-methyl, and a small percentage of unidentified residues. In rice, the parent compound generally comprises a larger percentage of the total extractable residues. A brown rice study at low moisture content showed that extractable residues consist of about 90% parent, 5.1% hydroxypyrimidine metabolities and ca. 4.5% mostly unidentified. Even at intervals exceeding one year, the parent compound may comprise the majority of the terminal residue.

In conclusion, actual residue levels in treated grains may be somewhat below the tolerance (i.e., application rate) if grains are stored for long periods of time. RCB again recommends that TAS calculations be carried out so that the residue levels in bread, bran and germ given in table I can be used to estimate dietary exposure.

ICI Issue No. 3

"We believe that the Agency's May 6 dietary exposure assessment (TAS computer analysis) significantly overstimates dietary exposure. Residue data previously submitted to the Agency will provide a more realistic dietary exposure if assessed on anticipated cholinesterase inhibiting residue rather than tolerance level residues. The Agency has regulated other compounds on this basis; however, we are not aware if the Agency has considered this for ACTELLIC. ICI expects to provide the Agency with our analysis of anticipated residues within the next several days.

RCB's Comments/Conclusions re: Issue No. 3

Since pirimiphos-methyl is relatively stable on stored grains, the anticipated level of cholinesterase-inhibiting residues in the raw agraicultural commodity (stored grains) should be the application rate.

RCB recommends that the Agency consider the maximum concentration factors presented in the M. Firestone memo of June 20, 1986 and reiterated in RCB's comments/conclusions re: Issue No. 2 - part D of this review.

Recommendation

RCB continues to recommend for establishment of the proposed pirimiphos-methyl tolerances for stored grains, their processed fractions, and animal commodities, as discussed in RCB's memo of May 7, 1986, TOX considerations permitting (note: RCB continues to conclude that the tolerance for a stored grain use should be set equal to the maximum application rate).

cc: RF,Circu,MPFirestone,PMSD/ISB,PP#3F2897/FAP#3H5399
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